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SARCOMA OF THE SMALL INTESTINE.

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During the past two years there have been observed at the Mount Sinai Hospital five cases of intestinal sarcoma, four of which came to autopsy. In three of these cases the clinical picture closely resembled that of appendicitis. In attempting to ascertain whether such a resemblance had before been noted, I found that not only was the clinical picture unknown, but also that there had been no complete review of the subject of sarcoma of the intestine since Baltzer wrote his article in 1893.

In the following paper I shall give the details of the four cases of ours which came to autopsy, and refer occasionally to the fifth case. I shall then attempt to give a complete picture of the disease from all its stand-points. I am indebted to Dr. Gerster for his kindness in permitting me to observe four of these cases clinically, to Dr. Lilienthal, in whose service the fourth case occurred, and to Dr. Brewer, by whom it was operated upon.

Case I.—H. G., aged twelve years, schoolboy, admitted September 30, 1898. History is of nine days' duration. The boy first complained of pain in the abdomen, below and to the right of the umbilicus, and of weakness. Three days ago abdominal distention was noticed, and since then there is marked constipation. The distention and pain have increased, and the boy suffers from dyspnœa.

On admission the temperature was 100.6°. The status in short was the following: Superficial abdominal and thoracic veins distended. Liver: upper border of dulness at fifth space, lower border undetermined. Abdomen much distended, signs of free fluid. Across the hypogastric region and extending into the pelvis there is a nodular tumor, concave above. Rectal examination revealed a large bulging mass anteriorly.

Operation, on October 1st, by Dr. Van Arsdale. The peritoneum was found lined with white nodular masses, and a large amount of chyliform fluid escaped. After the operation the boy gradually became weaker, there developed a left-sided empyema, purulent peritonitis, and otitis media. He died on October 29th.

Post-mortem Examination. (Abstract.) Lungs: large purulent exudate in left pleura. Small abscess in base of left lung. Infiltration of the diaphragm and base of the left lung by new growth. Evidences of healed tuberculosis in the right lung. Spleen: infiltrations on surface.

Kidneys: in the medullary rays brown streaks looking like uric acid infarcts; growths on anterior surface. Pancreas: diffusely infiltrated. Liver: size normal; fatty; covered by flat growths, white in color, some of which involve the parietal peritoneum. The wall of the gall-bladder is uniformly infiltrated. The omentum and mesentery are very much thickened, due to infiltration by tumor masses. The mesenteric nodes are all very large, and on section are white, homogeneous, and dry. Stomach: walls diffusely infiltrated. Intestinal coils are bound together, by masses between which are sacculations of green pus. The parietal peritoneum is not involved, except over the liver. The intestinal coils are attached to the bladder by some of the growths. The walls of the colon and part of the ileum show a thin infiltration with the new growth, the mucosa not being involved. In the duodenum, eight centimetres from the pylorus, is a large growth which encircles the gut, and projects into its lumen. The growth measures seven centimetres in length, five in width, and six in thickness. It encircles the gut, and projects into its lumen; the mucosa is intact. Microscopical examination: lymphosarcoma. (Some of the details of the microscopical findings will be given later.)

Notes. In this case of sarcoma of the duodenum, with extensive metastases, there existed stenosis of the intestine, which, as we shall later see, is the exception to the rule. The case was sent into the hospital with the diagnosis of "appendicitis." The diagnosis made in the hospital was "new growth of the peritoneum, probably sarcoma."

Case II.--A. R., aged three and one-half years, admitted December 23, 1898. History of eight days' standing. The child complained of abdominal pain, and the abdomen was seen to be enlarged and rigid. Bowels moved freely, but there was difficulty in urination. During the last three days the child vomited several times, and was feverish. The feet were not swollen.

The physical examination revealed the following: The liver flatness begins at the sixth rib, and extends four centimetres below the free border. Spleen is enlarged to percussion. The right side of the abdomen is occupied by an irregularly-shaped mass extending to the median line, easily pushed about, moving freely with respiration. The lower limit seems to be at the umbilicus. The surface feels irregular, as if the mass were composed of lymph nodes. The abdomen is symmetrically distended. There are some hard, round masses to be felt just above the groins. Temperature 100.8°.

25*th*. Urine contains considerable indican. Catheterization found necessary. Blood examination shows a moderate secondary anæmia and moderate polynuclear leucocytosis.

31*st*. Abdominal distention more marked. Intense dyspnœa.

January 5*th*. Operation by Dr. Gerster. Peritoneum found very much thickened. Some ascitic fluid escaped. The intestines were found adherent to each other, and to the omentum. The patient died on the following day.

Post-mortem examination showed the following changes: Lungs: large effusion of clear fluid in the left pleura. Abdomen: very much distended. The mesentery and omentum are everywhere thickened and whitish. All the intra-abdominal lymph nodes are enlarged, some being

four centimetres in diameter. On section they are white, succulent, soft. In the beginning of the ileum there is a large, white tumor infiltrating the wall, especially opposite the mesenteric attachment. The main tumor mass measures seven by eight centimetres, and is about three centimetres thick. On opening the intestine the growth is found to be indurated, and has an elevated irregular edge. Except for a few small areas of necrosis the mucous membrane is intact. The part of the ileum involved is considerably dilated, the circumference there being three times as great as that of the uninvolved part of the intestine. There is also an infiltration of the wall of many of the intestinal coils, and the coils are adherent to each other. The iliac lymph-nodes are very much enlarged and adherent to the bladder wall, which is much thickened and nodular. The ureters are partially obstructed by the tumor. The parietal peritoneum is involved, but to a lesser degree than the mesentery and omentum. Spleen: moderately enlarged; few nodules on the surface; slight infiltration along the vessels coming from the hilus. Pancreas: entirely infiltrated and very much enlarged. Kidneys: normal in size; cut surface yellowish. In the left kidney there are a few small nodules. The pelves of both kidneys are somewhat dilated, the left more than the right. Left adrenal entirely replaced by new growth, and adherent to the pancreas. Stomach: wall whitish and thickened. Liver: very much enlarged. Almost the whole right lobe is light brown in color, and is separated from the normal liver tissue by a raised edge. This lighter part is hard on section, and appears to be uniformly infiltrated by new growth. There are also a number of small, hard nodules present. The liver as a whole is somewhat fatty. Gall-bladder: distended with a colorless mucoid fluid; the neck of this organ is much thickened by new growth, and the cystic duct is impassable. Appendix is eleven centimetres long; the wall is much thickened and uniformly infiltrated with new growth. Bronchial nodes present the same appearance as the intra-abdominal nodes. Microscopical examination: lymphosarcoma.

Notes. This second case is an instance of a primary intestinal sarcoma with dilatation and with the most extensive metastases yet reported. The diagnosis before operation wavered between sarcoma of the kidney, tubercular peritonitis, and sarcoma of the peritoneum, with a possible primary intestinal tumor. The clinical history, except for the bladder symptoms, was rather typical.

Case III.—M. G., aged eighteen years; Russia; admitted January 22, 1899. History is of one day's standing; began with abdominal pains, most marked on the right side below the umbilicus. Bowels moved yesterday. Has been vomiting since last night, vomitus being bile-colored. No history of any previous attacks. Status: Hippocratic appearance; breathing rapid and shallow; pulse almost imperceptible; legs drawn up; abdomen tense and hard, uniformly tympanitic. By rectum a large doughy mass is felt high up. *Operation* by Dr. Van Arsdale. Saline infusion. The abdomen was opened in the right iliac fossa, and a large amount of fluid, fecal matter, and serum poured out. The appendix was found normal. The abdomen was then opened on the left side, and the peritoneal cavity irrigated.

Temperature on admission 103.6°, respirations 50, pulse 100, almost imperceptible. Freely stimulated. After operation pulse rapidly gave out.

The *autopsy* showed the following: In the jejunum, one and one-third metres from the duodenum, is a perforation in the intestine measuring seven by eight centimetres in diameter, with an irregular edge. The perforation is due to a tumor which has infiltrated the wall of the intestine and dilated it. The growth is white and soft on section, and varies from one-half to two centimetres in thickness. The tumor surrounds the circumference of the intestine, except for a space of three centimetres on the mesenteric side. Just above the tumor in the mesentery anteriorly is a node which looks cheesy. Posteriorly there is a lymph node infiltrated with sarcoma. There were no metastases found.

Microscopical examination of the tumor and the infiltrated nodes shows lymphosarcoma.

NOTES. This unique case is an instance of intestinal sarcoma which produced no marked symptoms until perforation occurred. The diagnosis of general peritonitis, probably due to perforation of the appendix, had been made.

CASE IV.—M. M., aged forty-two years, admitted January 8, 1900. For the last two weeks the patient has had irregular abdominal pain. During the past week he has suffered from frequent urination. No blood was passed, nor was there a urethral discharge present. Four days ago he was seized with severe abdominal pain, especially marked in the pelvis. There has been absence of fever, chills, and vomiting. The bowels were constipated until yesterday, although cathartics and enemata had been used. Within the last four days the patient has noticed a mass low down in the abdomen, which has grown rapidly and has become very tender.

The physical examination of the emaciated patient revealed an irregular tumor in the hypogastric region, extending into both iliac fossæ, especially the right. The tumor is quite tender, rather hard, but gives the sense of deep fluctuation. The rectal examination shows a hard symmetrical bulging. The temperature was 101.4°; the urine contained albumin, pus cells, and hyaline and pus casts.

Operation on day of admission by Dr. Brewer. On opening the abdomen a very large hemorrhagic tumor was found springing from the ileum and adhering to the right iliac wall, the floor of the pelvis, the large vessels, and the bladder. After much difficulty the tumor, together with two inches of the small intestine, was removed, and a Murphy button anastomosis performed. The patient died three days later from acute peritonitis.

The description of the tumor is as follows: It springs from the ileum at a distance of seventy centimetres from the valve. At its point of attachment to the intestine there is a beginning diverticulum. The tumor is very irregular in shape, and consists in general of two more or less reniform parts. The greatest width of the tumor is fifteen centimetres, the length thirteen centimetres, and the thickness eight centimetres. One-half of the growth is entirely hemorrhagic and cystic,

and the other half is necrotic and cystic. On cutting the tumor open it is found to begin in the submucosa, reaching to the mucosa, but not involving it. Microscopical examination : spindle-celled sarcoma.

Of the *autopsy* notes only the following are of special interest : The spleen shows acute inflammation and hemorrhages. The kidneys show chronic nephritis, with acute degeneration. In the liver there is a marked pigmentation presumably due to absorption of blood from the tumor. There are no metastases present.

NOTE. This case was one of a solitary tumor of the intestine, which clinically bore the closest resemblance to acute appendicitis, the acuteness of the symptoms being due in all probability to the hemorrhagic extravasation.

ETIOLOGY. *Frequency.* A glance at some statistics will be necessary to show the frequency of sarcoma of the intestine, and the comparative frequency of sarcoma and carcinoma. From 1859 to 1875 there was no case of intestinal sarcoma observed in the Berlin Pathological Institute. On the other hand, Smoler reports thirteen cases in Prague in fifteen years among thirteen thousand and thirty-six autopsies. Nothnagel states that in twelve years there came to autopsy in Vienna twelve cases of intestinal sarcoma. This certainly indicates that the disease is an unusual one. Possibly the occurrence of four cases of lymphosarcoma in our service in a very short time would tend to show that we may have to deal with an endemic disease, for, as we shall later see, there is reason to suspect these tumors to be of infectious origin.

Compared to the total number of lymphosarcomata the intestinal cases are not very infrequent. Nothnagel's figures show that among two hundred and seventy-four sarcomata three involved the intestine, and of sixty-one lymphosarcomata nine were primary in the intestine.

As to the frequency compared to carcinoma, Mueller reports five hundred and twenty-one cases of carcinoma, of which forty-one occurred in the intestine, and one hundred and two cases of sarcoma, with only one instance of intestinal involvement. Similarly, Nothnagel's figures show that among two thousand one hundred and twenty-five carcinomata two hundred and forty-three occurred in the intestine ; of two hundred and seventy-four sarcomata three occurred in the intestine, and among sixty-one lymphosarcomata there were nine of the intestine. So that sarcoma of the intestine is much more uncommon than carcinoma.

Location. Sarcomata have their seat of preference in the small intestine. In the large intestine they are much more uncommon, except in the rectum, where they occur quite as frequently as in the small intestine. A few figures will illustrate this. Krueger gives the following statistics of thirty-seven cases : Small intestine, sixteen ; ileum and

cæcum, one; cæcum, two; appendix, one; transverse colon, one; small and large intestine, one; rectum, sixteen. Nothnagel's figures are as follows: Of nine lymphosarcomata one involved the duodenum; three the jejunum; three the ileum, and two the cæcum. Of three sarcomata one occurred in the ileum; one in the cæcum, and one in the rectum.

Age. Baltzer states that 58 per cent. of the cases occur in the fourth decade, and in eleven of his fourteen cases the age was not over forty. I have collected fifty-one cases in which the age is noted. The results are as follows: First decade, six; second, nine; third, thirteen; fourth, thirteen; fifth, eight; sixth, one, and seventh, one. This shows that the age cannot be used as a diagnostic point. The oldest patient was seventy (Smoler). The youngest was a congenital case reported by Stern. This case was that of a child which died when five days old with symptoms of intestinal obstruction. There was found at autopsy a round-celled angiosarcoma of the jejunum.

Sex. Baltzer's cases, with one exception, were all males. I have collected fifty-nine cases including Baltzer's. Among these we find thirty-five males and fourteen females; or, in other words, the disease seems to be more than twice as common in males as in females.

Cause. As to the causation but little is known. In several instances the disease developed after a trauma, the usual interval until these symptoms developed being five to six weeks (Jalland, Pepin). In one case there is a previous history of syphilis. In another (Nothnagel) it followed a tuberculosis of the intestine. Flexner, in reporting two cases, drew attention to a histological feature of the growth, which he believed might throw a hint as to the cause of lymphosarcoma. He found in the growth in the stomach, intestine, and kidneys (most distinctly in the last) certain peculiar bodies. These were oval, round, or slightly irregular in shape, and consisted of a rim of protoplasm staining faintly with eosin, and enclosing a particle staining with hæmatoxylin. The last was oval or crescentic, and lay either in the centre of the cell or eccentrically. The bodies were distributed irregularly in the diseased areas, and an occasional body was seen in the adjacent parts. Flexner believed that they were probably protozoa, but stated that they might have no causal relationship.

I have found these bodies in the sections from the involved organs in our cases of intestinal lymphosarcoma, and also in specimens from other cases of lymphosarcoma. Although in places they at first impress one as probably being fragments of cells disintegrated by the infiltration of the new growth, a careful examination shows that such a view is not tenable, and one must agree with Flexner's view that they are at least suspicious.

Pathology. *Location and Size.* I have collected forty-two cases in which the location is given. Of these, fifteen occurred in the duod-

enum ; eighteen in the jejunum ; two involved the jejunum and ileum ; fourteen the ileum, and three the entire intestinal tract. These figures show that the larger number of sarcomata occur in the jejunum and ileum, but they may be located anywhere. The tumor may be single or multiple, small or large.

Varieties. The varieties of tumor found are : spindle-celled sarcoma, lymphosarcoma, myosarcoma, endothelioma interfasciculare, round-celled sarcoma, melanosarcoma, and mixed-celled sarcoma. Some round-celled sarcomata might better be classed with the lymphosarcomata.

When sarcoma occurs in the intestine it is generally primary there. It may, however, be secondary, or it may be part of a general lymphosarcomatosis. In this article we shall direct our attention to the primary cases only. In most of the cases the growth is confined to the mucosa and muscularis, and the serous coat is entirely or nearly entirely free. In a very few instances the growth began in the serosa, and later involved the inner coats. The lymphosarcomata, which formed the largest group (seventeen cases), generally begin in the submucous lymphatic nodules, and have a tendency to grow longitudinally. The muscularis is early infiltrated and paralyzed, and the feces dilate the intestine. This dilatation is a peculiar though not a constant feature of intestinal lymphosarcoma.

Metastases. I have arranged these according to the character of the growth. Among the cases reported with microscopical examination there are five instances of spindle-celled sarcoma. Four of these had no metastases ; one had metastases in the peritoneum and liver. The location of the tumor is not always given, but one was in the ileum, and our case was also in the ileum. Of the lymphosarcomata (seventeen cases) three involved the duodenum ; four the jejunum ; three the ileum ; one the appendix ; one the ileum and jejunum, and one the whole intestinal canal. Metastases occurred as follows : In three cases there were none ; in most of the cases the mesenteric nodes and other parts of the intestinal walls contained growths. The liver was involved seven times ; the kidney seven times ; the spleen three times ; the pancreas once ; the adrenals once ; the diaphragm twice ; the rectal wall twice, and the bladder four times.

Among the numerous other reported cases we will give details of a few only. In the case of Nicolaysen (myosarcoma) a few nodes in the mesentery were involved, and in Lehmann's case of endothelioma the whole intestine except twelve inches was involved. Of the round-celled cases (four) two involved the jejunum and two the ileum. In one case there were no metastases ; in another there were growths in the mesentery, and in the third the kidneys and upper part of the rectum were infiltrated. In Treves' case of melanosarcoma of the ileum the inguinal glands were infiltrated.

These data all go to show that the spindle-celled sarcomata have few or no metastases. The lymphosarcomata generally have extensive metastases, every abdominal organ and tissue being liable to invasion. The superficial lymph nodes are not generally involved. The metastases occur most commonly in the peritoneum, lymph nodes, liver, and kidney. There is a marked tendency for the growth to occur in the pelvis or for the original tumor to become adherent there. In our first two cases the growths seem to have been more extensive than in any other cases hitherto reported. A careful examination of the specimens showed that the growth extended almost entirely by continuity, or by contact. In the liver the growth extended inward from the surface, or along the vessels. The spleen and kidneys showed the same.

The parietal peritoneum was implicated only by extension from the visceral peritoneum. This opposes the statements made about the discontinuous growths of the lymphosarcomata, and strengthens the impression that these growths are infectious in nature, and that we are not dealing with metastases in the true sense of the word.

Microscopical Examination. I shall confine myself here to a few notes of my own cases. The fourth case needs but little commentary. In the other three cases the picture was that of a typical lymphosarcoma. I might mention, however, the great number of large lymphatic capillaries in some of the growths, and the frequent occurrence of the growth in the lumina of these capillaries.

In the first case the main growth was found in the submucosa, and through slits in the muscularis mucosæ the sarcoma cells reached up between the tubules. In some places the muscularis was entirely replaced by new growth. In the mesentery, omentum, and intestinal wall the tumor seemed to pass along under the serosa. The mucosa of the intestine above and below the growth showed no particular changes. The liver showed acute degeneration and congestion. The infiltrations in it followed the vessels, and tended to surround the lobules. There was some increase of the connective tissue between the lobules in the parts of the organ which were not infiltrated. The capsule was distinctly thickened. In the kidneys there was present a marked degeneration and congestion.

In the second case the sarcoma cells could very frequently be seen in the lymphatics. The liver showed fatty degeneration and infiltration and acute congestion. The growth seemed to spread between the liver cells, and at the edge of the infiltration the liver cells were almost entirely replaced by fat, or appeared to be necrotic. Near the growth the bloodvessels were much dilated. At a distance from the growth there was a marked parenchymatous degeneration, but less fatty infiltration. In one place there were small calcific deposits. The spleen was congested and hemorrhagic. The infiltration spread

here also along the connective tissue and around the vessels, and there could frequently be seen an infiltration about the vessels in the Malpighian bodies. In the kidneys there was found an acute congestion and degeneration. The infiltration occurred between the tubules, and in the areas involved the tubular epithelium was very indistinct. The stomach was diffusely infiltrated, even the mucosa being involved. In the gall-bladder the infiltration involved the submucosa only. The mucosa of the intestine above and below the primary growth for a short distance stained homogenously and showed no distinct structure.

In the third case there was a cheesy gland in the mesentery, but microscopically this proved to be lymphosarcomatous in nature. In the fourth case we will note only that the liver was markedly pigmented, that the kidney showed an acute parenchymatous degeneration, that the spleen was acutely inflamed and hemorrhagic, and that the heart presented a brown atrophy.

I have given the microscopical report of these cases to bring out the following points :

1. The transmission alongside the vessels, and the growth in the lymphatics in the lymphosarcoma cases.

2. The marked degeneration in those portions of the liver next to the new growth. Schulz (*Archiv für Heilkunde*, Band xv., p. 193) cites several instances of lymphosarcoma of the liver, stomach, intestines, and kidneys in which the epithelium near the growths was swollen, very granular, often fatty and disintegrated.

3. The parenchymatous degeneration of the liver and kidneys as a whole. In our second and fourth cases this must be explained as being due to the absorption of toxins or allied substances from the growths, and this again points to their probable infectious nature.

4. The fact that a cheesy gland may be lymphosarcomatous (*infra*).

5. The brown atrophy of the heart in the last case indicates a long continuance of the growth before the occurrence of distinct symptoms.

Flexner noted in his two cases extensive atrophy of the mucosa of the entire intestinal tract. In our case no such change was present, except to the slight degree noted in the second case.

Results of the Growth. (*a*) *Dilatation and Stenosis.* As pointed out by Kundrat, Treves, and Baltzer the lymphosarcomata cause dilatation of the intestine. This may be aneurismatic in form, as in the cases of Haas, Bessel-Hagen, and in our second case. Occasionally the tumor causes stenosis, but there is no case on record of complete stenosis due to obturation of the lumen by the tumor. Rutherford stated that the higher up the tumor lies the less likely is there to be stenosis. But we have noted that the stenoses have been found most commonly in the sarcomata of the duodenum. When a complete obstruction has been found it has been due to one of the following causes :

(1) Invagination (Wallenberg); (2) twisting of the mesentery, due to the tumor being caught in a hernial sac (Waldenström); (3) adhesions (Schmidt). The tumor may be attached to the intestine by a pedicle, as in Lannelongue's case. In our fourth case the tumor had produced a small diverticulum in the wall by traction.

(*b*) *Results of Compression.* The tumor may compress:

1. The vena cava, causing œdéma of the legs and ascites.

2. The bile ducts, and pancreatic duct (Lancereaux, sarcoma of the duodenum). In our second case the cystic duct was obstructed.

3. Ureters. This occurred in our second case, and resulted in a hydronephrosis of a moderate grade.

(*c*) *Ulceration and Perforation.* Ulceration is quite common, and may result in perforation, such perforation being either closed off by intestinal coils, the bladder or rectum, or opening directly into the general peritoneal cavity. The perforation may occur in any part of the intestine. The ulceration may expose vessels (Rolleston, sarcoma of the duodenum, erosion of the inferior pancreatico-duodenal artery). It is possible for these tumors to rupture without ulceration (Zuralski).

(*d*) *Changes in Other Parts of the Body.* The general changes and metastases have been described above. The pleural cavities may contain clear fluid or pus. There may be a localized or general peritonitis, the effused fluid being chyliform, clear, purulent, or hemorrhagic. There are practically no reports of a careful examination of the effusions in these cases. In the case reported by Henoch the fluid was hemorrhagic and contained numerous round cells showing fatty degeneration. We shall later give the details of the fluid in our fifth case.

(*e*) *Connection with Other Diseases.* In one case there was found a mixed-celled sarcoma of the ileum and an adenocarcinoma of the pylorus (Smoler). More important is the fact that lymphosarcoma has frequently been found in persons having either an intra-abdominal tuberculosis or a florid or healed tuberculosis elsewhere. The exact connection is not understood. While not attempting to state that a combination of tuberculosis and lymphosarcoma is not frequent, we believe that only cases in which a microscopical examination is reported should be credited, for just as Sternberg has shown, that a lymph node that looks lymphosarcomatous macroscopically may be tubercular on microscopical examination, so I have shown that the opposite mistake can be made.

Symptomatology. *General Description.* Nothnagel gives us a good outline of the disease when he states that there is very early and without exception a marked affection of the general system and but few local symptoms. Baltzer's description, which has been quoted in most of the books, is as follows (abstract): "The symptoms are very slight at the onset. There is at first pain in the stomach, loss of appetite, nausea, vomiting; the bowels are irregular, being either constipated or

loose. The abdomen soon becomes distended. When seen early all the patients are very thin and have a pale color. A tumor is generally found, although it may be missed for a long time; it may be located in any part of the abdomen, and it is generally but slightly or not at all tender. The temperature is normal or moderately elevated. In some cases there is a leucocytosis. The duration of the disease varies from two weeks to one and three-quarter years, but most of the patients died within nine months."

Detailed Symptomatology. *Pain* is present in practically all the cases. It may be mild or severe, and may be located in any part of the abdomen. In most cases the pain is referred to the stomach, and occasionally it is especially marked after meals. In three of our cases the pain was specially referred to the region of the appendix.

Distention of the Abdomen is very common, being uniform or irregular. Its onset is frequently sudden, and the symptoms of the disease may date from its appearance. The swelling may rapidly increase or remain at a standstill, later to become suddenly more marked. The distention is due either to involvement of the peritoneum, pressure on the vessels, perforation of the intestine, tympanites, or the size of the tumor. If fluid is present it may be clear, chylíform, purulent or hemorrhagic. In our first case it was chyliform, in the second clear, and in the third fecal. In the fifth case a paracentesis abdominis was made, and the fluid showed the following: It was cloudy, yellow, odorless; its specific gravity 1014. There was present a trace of urea; albumin, 0.12 (.1290) per cent. Microscopically there were found a large number of pus-cells, red blood-cells, and some epithelial cells, numerous cocci and bacilli. Culture showed the bacterium coli commune.

Characteristics of the Tumor. In some cases a tumor cannot be made out. If a tumor is discovered it may be first found by examination, or it may be the symptom which leads the patient to consult a physician. After the tumor is once there it may grow very rapidly. The growth may be large or small, single or multiple. The lymphosarcomata often feel like one irregular tumor, whereas in reality the growth in the intestine is very small, and the irregularity is due to growths in the peritoneum and lymph nodes. At times small nodules are found which feel like lymph nodes, but which on post-mortem examination prove to be infiltrated appendices epiploicæ. The tumor may be superficial or deep. It may be possible to feel one large tumor and scattered nodules all over the abdomen, some feeling as if they were in the parietal peritoneum. Such an observation was made in our second case.

The tumor is generally only slightly or not at all tender. Marked tenderness occurred in only one of our five cases. The growths usually move with respiration, and can generally be moved around in the abdo-

men. The note over them is generally dull or dull tympanitic. Their consistency is generally moderately hard, although very soft and very hard ones have been described. The centre may show indistinct fluctuation, as in our fourth case. Crepitation may be felt over the tumor, and the latter may be seen to take part in the peristaltic movements of the intestine.

The position of the mass is most variable, but a large number of them tend to grow downward, or the growth occurs primarily in the lower part of the abdomen. As a result a rectal examination may reveal a tumor when nothing or only small nodules can be felt in the abdomen. In three of our cases parts of the growth could be felt by the rectum.

Symptoms Due to Compression. These may be summarized as follows: 1. Ascites or œdema of the legs and scrotum, the latter two being important symptoms. 2. Distention of the veins of the abdominal and thoracic walls. 3. Jaundice and alcoholic stools. 4. Dysuria and diminution in the amount of urine.

Gastric Symptoms. Loss of appetite and vomiting are of frequent occurrence. The vomited matter may contain bile, especially if the tumor is high up, but vomiting of blood is exceptional, except when as a terminal symptom. In our fifth case hæmin crystals were found in the vomitus comparatively early in the disease. In Stern's congenital case meconium was present. The gastric pains have been referred to.

Intestinal Symptoms. There is generally some disturbance in the movements of the bowels, although the exact character varies. Thus there may be always constipation or always diarrhœa. There may be first constipation, and then diarrhœa, or they may alternate. More characteristic is an early diarrhœa followed by persistent constipation. The constipation is not absolute, except when some complication is present, as already referred to. Rarely "erections of the intestine" may occur (Schmidt). The movements may contain pus and blood, although the admixture of blood generally speaks for involvement of the large intestine.

Hepatic Symptoms. The liver has generally been described as not being enlarged, but in three of our cases there was quite marked increase in size. Rarely jaundice is present.

Pulmonary Symptoms. Dyspnœa is not uncommon, being due to pleural effusions, the abdominal distention, or the weakness and anæmia. The pleural effusion is bilateral or unilateral, and the fluid is serous or turbid or hemorrhagic.

Urinary Symptoms. The urine may be scanty and contain much urates. Albumin is frequently present, pus and blood rarely. There may be difficulty in urination of even marked degree, as in our second case. The urination may be very frequent and painful.

Cutaneous Symptoms. Sweating is not uncommon, especially at night.

The œdema of the legs and scrotum, due to pressure or hydræmia, may occur quite early. There may even be a general slight anasarca. The veins of the abdominal wall and thoracic walls may be prominent. Of great importance is the appearance of a peculiar white color in the face, which may come on suddenly, and usually appears after the abdomen is distended. This rather characteristic color appeared in our first two cases very early, but in the fifth case it was first noted a few days before death.

External Lymph Nodes. These are not generally enlarged. But in a case of melanosarcoma of the ileum, reported by Treves, there was a swelling in the left groin which was suspected of being a hernia, but which proved to be a lymph node containing metastases.

Temperature. The temperature may be quite normal throughout the disease, but is more common to find evening rises to 101°, 102°, or 103°. Our cases all had febrile movements.

Emaciation and marked loss of strength are generally prominent features. They were present in all our cases, but developed in the fifth case very late.

Blood Changes. Here there is nothing characteristic, although anæmia and leucocytosis have been described. Schmidt made a careful examination of the blood in two cases, and noted in both a diminution in the amount of fibrin and an increase in the number of hæmatoblasts. In our second case an examination showed a moderate secondary anæmia, with slight polynuclear leucocytosis.

Course of the Disease. A consideration of the symptomatology as just given will show that the descriptions given by Baltzer and Nothnagel will not fit many of the cases. I have therefore endeavored to classify the varieties of the disease in the following way:

1. Latent cases, the disease being first discovered at autopsy.
2. Cases with the clinical picture described by Baltzer, either the general symptoms, the distention of the abdomen, or the tumor being first noted.
3. Cases in which the first symptoms are due to an intussusception or other variety of intestinal obstruction or to perforation.
4. Cases resembling tubercular peritonitis.
5. Cases in which jaundice is the first symptom.
6. In one case there was the closest resemblance to an ovarian cyst.
7. Finally, the cases may bear a very close resemblance to appendicitis, an observation made for the first time in our cases.

Diagnosis. Of all the symptoms just detailed the following are important for the diagnosis: the presence of a tumor (rectal examination) which is not markedly tender, abdominal distention, absence of symptoms of stenosis, early œdema of the legs, the lack of involvement of the external lymph nodes, the emaciation, the peculiar color, the absence

of marked ascites. But none of these symptoms is absolutely constant. It is very difficult to establish any exact rules for diagnosis, as any one observer is apt to see but few cases. We shall endeavor to give a few hints and to indicate the diseases with which intestinal sarcoma is most likely to be confounded, omitting the very rare conditions, such as actinomycosis or echinococcus disease.

The main question that arises is, Can these tumors ever be positively diagnosed? Undoubtedly in many cases it would have been impossible to make the correct diagnosis. We believe, however, that in a certain number of instances the correct diagnosis can at least be strongly suspected. If there is a large movable tumor present, or, better, one large and several small tumors, or, if beside, growths can be felt by rectum, with but little or no ascites, and with early œdema of the legs, and the peculiar color described, the diagnosis of sarcoma of the mesentery or omentum is very probable. If these symptoms occur in a person under fifteen the diagnosis is still more probable. Having made a diagnosis of peritoneal sarcoma, and the tumor being movable, the existence of a primary intestinal sarcoma must be strongly suspected, and can be made positively if there exist early in the case intestinal disturbances, or if the colon bacillus can be isolated from effused fluid, if such be present (as in our fifth case). Of course we can never say positively that the tumor is not primary in the mesentery. However, as far as treatment is concerned, there is no importance in this distinction.

The following are the diseases to be differentiated:

1. *Carcinoma of the Intestine and Peritoneum.* Baltzer states that sarcoma occurs earlier in life, that carcinoma is apt to produce a stenosis earlier, is more tender, and lasts longer. Schmidt believes that œdema of the legs, with little or no ascites, would favor sarcoma. This latter statement is certainly true. Baltzer's remarks are, however, not absolutely correct. We shall later see that, although sarcoma is usually rapid in its course, it may be slow, and there are numerous instances in which carcinoma runs a rapid course. Again, we have shown that sarcoma does occur after the fortieth year, although not commonly. According to our personal experience, carcinoma of the intestine occurs quite frequently in people between the ages of fifteen and twenty-five. It is true that it then generally involves the cæcum, descending colon, or rectum, but if metastases are already present (and it is mainly under such conditions that the differential diagnosis must be considered) the cases might well be confused with sarcoma of the intestine. We will therefore modify Baltzer's statement, and say that under fifteen years of age the diagnosis would be decidedly in favor of sarcoma (although it is true that even congenital intestinal carcinoma has been described as well as congenital sarcoma), and that after the age of forty sarcoma is less probable but cannot be excluded. Important points against the

diagnosis of carcinoma are the absence of external glandular involvement, the absence of tenderness, and the large size of the growths in the sarcoma cases.

2. *Tubercular Peritonitis, and Tuberculosis of the Mesenteric Lymph Nodes.* The differential diagnosis may be very difficult, and even if a positive diagnosis of sarcoma is made the presence of a concomitant tuberculosis cannot be excluded. This was made especially clear in a case described by Nothnagel, in which his diagnosis wavered between these two conditions, and in which the autopsy revealed lymphosarcomatous growths, springing from the edges of cicatrizing tubercular ulcers. The presence of a very large tumor or tumors speaks more for sarcoma. The facies is different in the two conditions, but the recognition of this point requires much experience. Ascites is more apt to occur early in tuberculosis. A tubercular history is of no use in excluding sarcoma, nor is the existence of fever. If the ascitic fluid should reveal tubercle bacilli of course the diagnosis of at least a tubercular condition being present would be absolute.

3. *Intestinal obstruction, intussusception or intestinal perforation when due to sarcoma,* is accompanied by the same symptoms as under other conditions, and the diagnosis can be made only if the growths can be felt and if other symptoms are present.

4. *Sarcoma of the kidney* is not generally so mobile. Hæmaturia would speak decidedly for a renal growth, but this does not occur in the majority of cases. In renal sarcomata the tumor is generally located more on one side of the abdomen, but this may also occur in intestinal sarcoma. If nodules are felt elsewhere in the abdomen they speak for intestinal or mesenteric sarcoma, as the renal cases do not show metastases in the peritoneum. Further, the kidney sarcomata are less rapid in their course.

5. *Ovarian Tumors and Cysts.* A pedunculated intestinal growth may closely simulate an ovarian cyst, and, on the other hand, an ovarian tumor may be located in the upper part of the abdomen, and simulate a mesenteric or intestinal tumor. The finding of a pedicle (Hegar's method) springing from the uterus would make the diagnosis clear. In a case recently seen no pedicle was felt (Hegar's method not being tried), and as the tumor was surrounded by a group of distinct nodules the diagnosis of intestinal or mesenteric sarcoma seemed assured. The operation, however, revealed an endothelioma of the ovary, and what had appeared to be separate nodules were found to be large irregularities springing from the tumor.

6. *Neoplasms of the Bladder and Prostate Gland.* Given a large tumor in the region of the bladder or prostate, especially in a person under forty, it is necessary to determine whether or not the same is

due to a secondary growth from an intestinal sarcoma or is a primary intestinal growth which has become adherent in the pelvis. In two of our cases some of the symptoms might easily have been construed as indicating a primary growth of the bladder.

7. *Retroperitoneal Sarcoma.* The differential diagnosis may again be very difficult here, although unimportant, for an intestinal tumor extensive enough to resemble one of these retroperitoneal sarcomata is generally a non-operable case. We cannot enter into a description of these sarcomata here, but would refer to a review of the subject by Steele, in THE AMERICAN JOURNAL OF THE MEDICAL SCIENCES, March, 1900, page 322. He says that in retroperitoneal sarcoma the colon lies in front of the tumor, that obstruction of the intestine is apt to ensue, and that pain in the legs and in the lumbar regions is characteristic.

8. *Appendicitis with or without Peritonitis.* Our third and fourth cases show how closely this may be simulated by an intestinal sarcoma (and it is not difficult to appreciate how much greater this similarity might be in cases where the sarcoma is primary in the cæcum). The diagnosis will have to be made on the lines laid down until more cases are reported. I would lay great stress, however, on the attempt to find nodules by rectal examination. A single mass felt by the rectum is not of much use for differentiating the conditions, as such a finding is frequently enough made in appendicitis cases, and it not uncommonly occurs that a separate, very hard mass closely resembling a tumor may be felt by the rectum in cases of appendicitis.

9. *Differential Diagnosis Between Lymphosarcoma and Other Varieties of Sarcoma.* This cannot at present be made with any degree of certainty; all we can now say is that with spindle-celled sarcomata there is apt to be one large mass, whereas the lymphosarcoma cases usually present multiple growths.

EXPLORATORY LAPAROTOMY. We believe that this is indicated in all cases except in those in which there can be felt several distinct masses at some distance from each other. A large mass with nodules nearby may represent a solitary tumor only, as was demonstrated in the case of ovarian endothelioma cited above.

DURATION AND PROGNOSIS. Baltzer puts the duration at from two weeks to one and three-quarter years, most cases dying within nine months. This statement is corroborated by the cases since reported with the exception of a case described by Rutherford, which was of two and one-half years' duration. In our third case the history was only of one day's duration, but the statement made by the relatives that the patient had slight pains in the stomach for three months, although he continued at work, must be taken to indicate a longer existence of the illness.

The prognosis seems to be almost invariably fatal. A number of these cases have been operated on, and some, it is claimed, with a favorable result, but the ultimate outcome of the cases has not been given. In only one instance—a case reported by Babes and Nanu—was the patient alive after one year, and the authors themselves state that the ultimate outlook was bad. The other operated cases are as follows: Nicolaysen: spindle-celled sarcoma; recurrence in twenty-four days. Zuralski: cystic sarcoma; recovery for the time being. Lannelongue: variety of tumor not given; ultimate result not stated. Heinze: resection of 110 cm. of the intestine with mesentery; recovery, but ultimate result not given. Among Baltzer's cases there are four in which death resulted within twenty-four hours after operation. Siegel has recently reported a case of lymphosarcoma for which he resected 30 cm. of small intestine, but death resulted within two weeks. Van Zwalenburg (verbal communication: case to be presented at the meeting of the American Medical Association, June, 1900) has operated on a case, the patient being alive now, seven months since the time of operation.

Treatment. (*a*) *Operative.* When the growth can be removed completely this should certainly be done; but we believe that cases of lymphosarcoma with extensive metastases should not even be subjected to exploratory incisions, as this is likely to hasten the occurrence of the fatal issue.

(*b*) *Medicinal.* In the literature there are a number of undoubted instances in which sarcomata, particularly lymphosarcomata, have been cured or improved by arsenic given internally, used hypodermatically, or parenchymatously (into lymph nodes). Such cases have been reported by Liebmann, von Ziemssen, Köbner, Billroth, Winiwarter, Tholen, Arning, and Wunderlich. In their cases there was generally present a multiple lymphosarcomatosis, or sarcoma of the skin. We believe that this treatment should invariably be tried in cases of intestinal sarcoma, and that it should be used also for the patients upon whom successful resections have been performed. Whether Coley's fluid would be of any value in these cases future experience alone can decide. The remainder of the treatment is purely symptomatic.

Addenda. Since writing the above my attention has been drawn to an interesting case reported by Lindner in the *Beiträge zur klin. Chirurgie*, 1899. This case was that of a man, aged thirty-six years, who six months before he came under observation was operated upon for a supposed carcinomatous ulcer of the head, and who for fourteen days was suffering from symptoms of ileus. There were present a marked enlargement of the lymph nodes on one side of the neck and a tumor in the right hypochondrium. At the operation an intussus-

ception of the small intestine was found, and the gut was full of lymphosarcomatous tumors. A resection was done, but the patient died after twenty-four days. Lindner believes that the tumor was primary in the intestine, and that the ulcer on the head, which had been supposed to be carcinomatous, was probably sarcomatous. He reports the case as an instance of a tumor whose metastases caused symptoms long before the primary growth was revealed, but does not state how long the tumors were present in the neck.

A case of intestinal sarcoma was reported to the Surgical Section of the New York Academy of Medicine by Dr. Weir, on May 14, 1900, for which he resected eight feet of small intestine. The patient lived for two days. Dr. Weir kindly allowed me to refer to this case before its publication in the Society reports.

Two further cases of lymphosarcoma occurred in the hospital in June, 1900.

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REVIEWS.

COLUMBIA UNIVERSITY BIOLOGICAL SERIES. Vol. IV. "The Cell in Development and Inheritance." By EDMUND B. WILSON. Second edition, revised and enlarged. New York and London: The Macmillan Co., 1900. Pp. xxi., 483, with 194 figures in the text.

THE importance of the cell theory in the medical sciences has been generally recognized since the appearance of Virchow's *Cellularpathologie* in 1858. Strange to say, however, medical men have paid extremely little attention to the cellular phenomena until within the last few years, and even now such attention is confined almost exclusively to certain cellular aspects of pathology. In this country, at least, medical education takes almost no account of the normal structure and functions of cells, and yet upon this very basis must rest any thoroughgoing knowledge of the animal body in health and disease. Verworn and Loeb have called attention to the necessity of a knowledge of cellular or general physiology if one is to arrive at any understanding of the fundamental properties of living things, and a similar claim may be made for cellular morphology. In fact, the cell theory of Schleiden and Schwann occupies a position in biology to-day second only to the evolution theory, and in some respects the former is even more fundamental than the latter, since the whole problem as to the mechanism and causes of evolution, inheritance, variation, assimilation, metabolism and irritability can be approached only from the stand-point of the cells.

To be sure, it is not absolutely essential that a physician should be trained in cytology in order to make diagnoses and write prescriptions. The structure or functions of nucleus or cytoplasm are of small concern to the man who is primarily interested in the art of applying to the recognition and cure of disease those principles which are already well established. On the other hand, a knowledge of cytology is indispensable to the medical man who is striving to extend the bounds of his science, and the history of medicine no less than the whole history of human advancement serves to show that no knowledge of fundamental phenomena is useless or without consequence.

The greatest danger in all recent scientific work is the outgrowth of the very principle which has made science most effective, viz., *specialization*. So great are the number of workers, and so rapid is the advance in every science, that it has become impossible for any one man to follow the whole advance of his own science. Louis Agassiz used to say that he pitied the man who would undertake to keep track of zoölogical literature fifty years after his day. There are few if any such men to-day either in zoölogy, botany, physiology, pathology or related sciences. Men are no longer naturalists, but helminthologists, ophthalmologists, cytologists, etc., and while the result of this specialization

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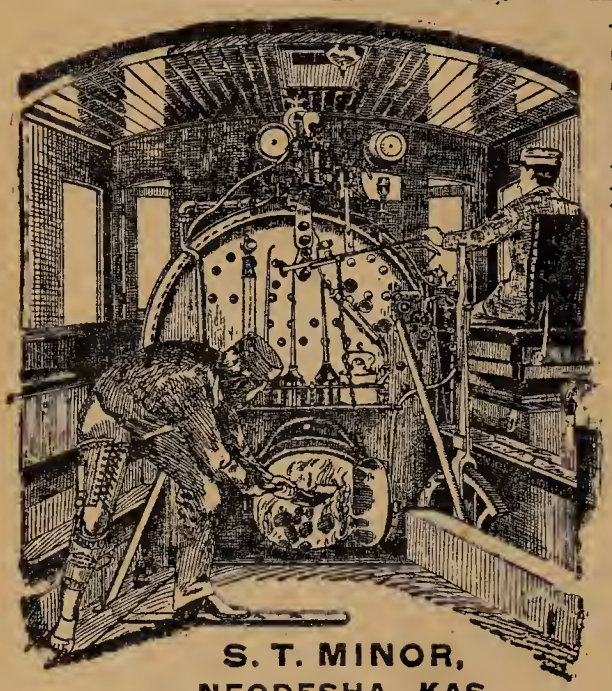

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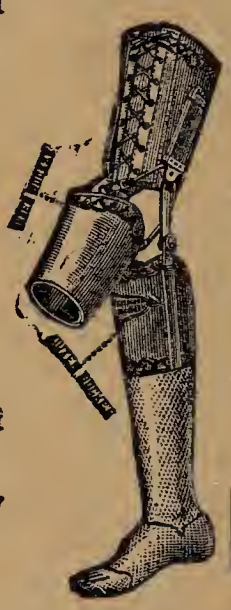

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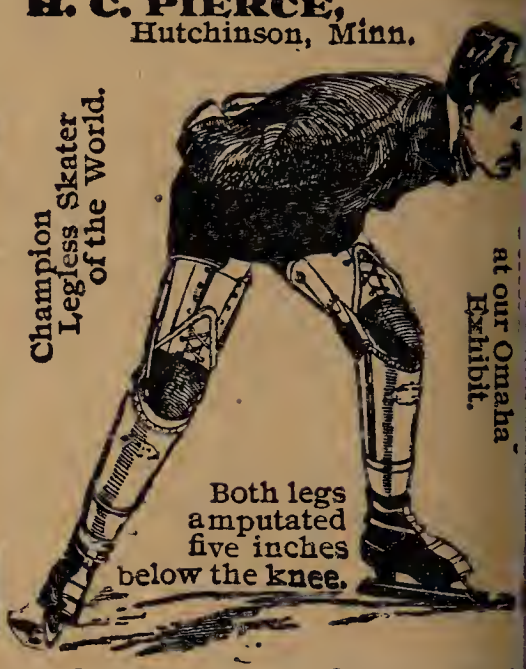

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